Phosphoproteomic analysis of human embryonic stem cells.

Journal: Cell Stem Cell

Publication Year: 2009

Authors: Laurence M Brill, Wen Xiong, Ki-Bum Lee, Scott B Ficarro, Andrew Crain, Yue Xu, Alexey Terskikh, Evan Y Snyder, Sheng Ding

PubMed link: 19664994

Funding Grants: Training Grant I

Public Summary:
Protein phosphorylation, while critical to cellular behavior, has been under-characterized in pluripotent cells. Therefore, we performed phosphoproteomic analyses of human embryonic stem cells (hESCs) and their differentiated derivatives. 2546 phosphorylation sites were identified on 1602 phosphoproteins; 389 proteins contained more phosphorylation site identifications in undifferentiated hESCs, whereas 540 contained more such identifications in differentiated derivatives. Phosphoproteins in receptor tyrosine kinase (RTK) signaling pathways were numerous in undifferentiated hESCs. Cellular assays corroborated this observation by showing that multiple RTKs cooperatively supported undifferentiated hESCs. In addition to bFGF, EGFR, VEGFR and PDGFR activation was critical to the undifferentiated state of hESCs. PDGF-AA complemented a sub-threshold bFGF concentration to maintain undifferentiated hESCs. Also consistent with phosphoproteomics, JNK activity participated in maintenance of undifferentiated hESCs. These results support the utility of phosphoproteomic data, provide guidance for investigating known and novel proteins in hESCs, and complement transcriptomics/epigenetics for broadening our understanding of hESC fate determination.

Scientific Abstract:
Protein phosphorylation, while critical to cellular behavior, has been undercharacterized in pluripotent cells. Therefore, we performed phosphoproteomic analyses of human embryonic stem cells (hESCs) and their differentiated derivatives. A total of 2546 phosphorylation sites were identified on 1602 phosphoproteins; 389 proteins contained more phosphorylation site identifications in undifferentiated hESCs, whereas 540 contained more such identifications in differentiated derivatives. Phosphoproteins in receptor tyrosine kinase (RTK) signaling pathways were numerous in undifferentiated hESCs. Cellular assays corroborated this observation by showing that multiple RTKs cooperatively supported undifferentiated hESCs. In addition to bFGF, EGFR, VEGFR, and PDGFR activation was critical to the undifferentiated state of hESCs. PDGF-AA complemented a subthreshold bFGF concentration to maintain undifferentiated hESCs. Also consistent with phosphoproteomics, JNK activity participated in maintenance of undifferentiated hESCs. These results support the utility of phosphoproteomic data, provide guidance for investigating protein function in hESCs, and complement transcriptomics/epigenetics for broadening our understanding of hESC fate determination.

Source URL: http://www.cirm.ca.gov/about-cirm/publications/phosphoproteomic-analysis-human-embryonic-stem-cells